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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/603,024	06/23/2000	Markus Pompejus	BGI-131CP	1349

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EXAMINER
FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/603,024	POMPEJUS ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *17-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 36-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. The Applicants election with traverse of Group I is acknowledged. The traversal is on the ground(s) that ten sequences are normally permitted. This is not found persuasive because the guidelines permit "up to 10" sequences. The current situation represents a burden on both the Office because each additional sequence will require separate analysis for utility, description and will require a different and extensive nucleic acid search by the Scientific and Technical Information Center. Therefore, the requirement is maintained and only a single nucleic acid, SEQ ID NO: 1, will be examined.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1-16 and 36-38 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The current claims are drawn to a genus of nucleic acids which encode a protein termed MCT, or portions thereof, in the specification, wherein the sequence cannot consist of F-designated genes.

Credible Utility

Following the requirements of the Utility Guidelines (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for Utility.), the first

inquiry is whether a credible utility is cited in the specification for use of the proteins. The cited utilities in the specification include modulation of chemical production and using the proteins to produce fine chemicals. These utilities are credible.

Upon identification of credible utilities, the next issue is whether there are any MCT protein or nucleic acid of SEQ ID NO: 1 are identified in either the specification or in the cited prior art.

Substantial utility

Given the absence of a well established utility, the next issue is whether substantial utilities are disclosed in the specification. Here, the evidence in the specification provided is that the protein is related to the ABC transporter family of proteins. This relationship lacks any of the hallmarks of utility. The homology does not imply that the proteins are similar in any function way, or that they are expressed in similar tissue types or under similar conditions. There is no biological activity, expression pattern, phenotype, disease or condition, ligand, binding partner or any other specific feature which is disclosed as being associated with the protein encoded by SEQ ID NO: 1. Without any further information, there is no expectation that the protein will have any properties in common with the ABC transporter protein. There is an abundance of evidence that very similar proteins can perform very different functions. For example, Rost et al (J. Mol. Biol. (2002) 318(2):595-608) notes regarding assignment of enzymatic activity based upon homology comparisons that "The results illustrated how difficult it is to assess the conservation of protein function and to guarantee error-free genome annotations, in general: sets with millions of pair

comparisons might not suffice to arrive at statistically significant conclusions (abstract)." Thus, even high levels of homology do not necessarily correlate with actual protein function. In the current case, where the function of MCT (SEQ ID NO: 1) is not known, the expectation is even lower that there is any utility that can be derived based upon this association.

This situation is extremely similar to example 12 of the Utility Guidelines, where a protein which was known to be a receptor, but where the ligand was unknown, was found to lack utility. In the current case, the putative MCT protein, as an ABC transporter, lacks a known ligand. Similar to the receptor in Example 12, it lacks a substantial utility because there is no "real world" context of use. The only uses are unspecified methods of making the protein or methods of producing undefined and unnamed fine chemicals using the protein. Further research would be required to identify and reasonably confirm a "real world" context of use. As noted in the utility guidelines, basic research on a product to identify properties and intermediate products which themselves lack substantial utility are all insubstantial utilities (see page 6 of the Utility guideline training materials).

Specific Utility

In the current case, even if the substantial utility argument above were found unpersuasive, there is no specific utility given for this MCT protein of SEQ ID NO: 1 and the resultant nucleic acid. The protein has not been associated with any disease, any condition, or any other specific feature. The only association is that it has some homology to a protein, the ABC transporter. As the utility guideline training materials

note on page 5-6, "Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed". Here, the homology to the ABC transporter gives no specific utility because ABC transporters represent a class of molecules which may export or import any of a variety of molecules ranging from lipids, polysaccharides and proteins to maltose or histidine (see Nikaido et al (PNAS (2002) 99(15):9609-9610). The class ranges to include a bacterial histidine transport protein and the human Cystic Fibrosis transmembrane conductance regulator (see Nikaido et al (PNAS (2002) 99(15):9609-9610). Therefore, there is no specific utility for this protein until a specific ligand is identified.

Finally, with regard to the utility analysis, the current situation directly tracks Examples 4 and 12 of the utility guidelines, where a protein of entirely unknown function and a receptor with an unknown ligand was characterized as lacking utility.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-16 and 36-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification, since the claims are not limited to any particular SEQ ID NO, but are open to a nucleic acid which encodes any protein named MCT, without any structure provided whatsoever. The claims are further open to any nucleic acid which encodes any portion of the MCT protein. For example, the specification does not teach the sequence of MCT1, a human monocarboxylate transporter, as shown in Genbank Accession Number NM_014060, which is different than SEQ ID NO: 1. Further, the specification does not teach the Emericella MCT gene of Genbank Accession Number AY236409. Each of these different nucleic acids is properly termed an MCT protein, but the specification lacks a description of their sequences.

Most significantly, the genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named SEQ ID No 1. Thus, applicant has express possession of

only one particular sequence in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains.

There is no showing or evidence which links structural limitations or requirements to any particular functional limitations. Further, these claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and only specific nucleic and amino acid sequences have been provided. No written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the nucleic acids as encoding an MCT protein lacks any specific structure, since it is in the absence of knowledge of the material composition.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound without identifying the structure function relationship of the compound, so that the compound is claimed solely by the functional utility of being a nucleic acid which encodes an "MCT protein" without any additional structural limitations.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise SEQ ID NO 1. Therefore, the claims fail to meet the written

description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 112 – Scope of Enablement

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 and 36-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to a nucleic acid which encodes the MCT protein. The invention is in a class of invention which the CAFC has characterized as "the

unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The claims broadly encompass not only the particular MCT encoding nucleic acid but also include any nucleic acid which shares that name, any portion of the protein, or 50% homology thereto.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant variability in the activity of polypeptides and nucleic acids. It would require significant study to identify the actual function of the MCT protein and nucleic acid, and identifying a use for this protein would be an inventive, unpredictable and difficult undertaking in itself. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The unpredictability of the art and the state of the prior art

The art is extremely unpredictable with regard to protein function in the absence of reliable information regarding the protein activity. Even very similar proteins, as shown by homology, may have very different functions (see Rost et al (J. Mol. Biol. (2002) 318(2):595-608). In the current case, where no specific information is known regarding the function of the protein in actual biological organisms, it is entirely unpredictable what function and activity will be found for this protein. The prior art does not resolve this ambiguity, since no prior art activity is identified for the protein.

Working Examples

The specification has no working examples.

Guidance in the Specification.

The specification provides no specific or substantial uses for the MCT protein. The specification does generically teach that the protein may be used in the production of fine chemicals but no specific chemical is identified, no specific ligand for the MCT protein is identified and no specific resulting product is identified.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the presence of a working example which does not address the issue of the efficacy of the control and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-8, 10-13, 15, 16, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Genbank Accession Number AF045938 (02 May 1998).

Genbank AF045938 teaches a nucleic acid sequence which encodes an ABC transporter gene which has 74% local similiarity with SEQ ID NO: 1 and which would hybridize to SEQ ID NO: 1 under stringent conditions. Genbank AF045938 comprises many portions of SEQ ID NO: 1, including, for example the 17 mer from nucleotides 123 to 140 of SEQ ID NO: 1. Genbank AF045938 teaches the sequence in a Mycobacterium host cell in the genome, which permits expression of the protein and which is modified. Genbank AF045938 inherently is involved in the production of chemicals in the cell which are organic in nature. Lastly, Genbank AF045938 inherently has one or more modifications from the sequence set forth in Appendix A.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 9, 14, 36 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Genbank Accession Number AF045938 (02 May 1998) in view of Ago et al (U.S. Patent 5,955,137).

Genbank AF045938 teaches a nucleic acid sequence which encodes an ABC transporter gene which has 74% local similiarity with SEQ ID NO: 1 and which would hybridize to SEQ ID NO: 1 under stringent conditions. Genbank AF045938 comprises many portions of SEQ ID NO: 1, including, for example the 17 mer from nucleotides 123 to 140 of SEQ ID NO: 1. Genbank AF045938 teaches the sequence in a Mycobacterium host cell in the genome, which permits expression of the protein and which is modified. Genbank AF045938 inherently is involved in the production of chemicals in the cell which are organic in nature. Lastly, Genbank AF045938 inherently has one or more modifications from the sequence set forth in Appendix A.

Genbank AF045938 does not expressly teach placing the nucleic acid molecule in a vector with a heterologous polypeptide, expressing in Corynebacterium, disrupting the nucleic acid, or using a heterologous regulatory region.

Ago teaches expression of a bacterial protein in vectors such as pBTac2 and pBTrp2 and pBluescript (see column 5, lines 11-16), each of which places the nucleic acid under the control of a heterologous regulatory region and in a vector with a

heterologous polypeptide such as an antibiotic resistance gene. Further Ago teaches expression in Corynebacterium and Brevibacterium (see column 4, lines 56-60). Lastly, Ago teaches disruption of nucleic acids to alter the expression level of the gene (see column 4, lines 35-38).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the nucleic acids of Genbank AF045938 as taught by Ago since Ago notes

> "Isolation of the gene of the present invention, determination of the nucleotide sequence of said gene, by preparation of the recombinant vector of the present invention and the transformant carrying the recombinant vector of the present invention, and production of the protein of the present invention can be carried out given the information provided herein by those of ordinary skill in this art using basic techniques for genetic engineering and biological engineering according to the descriptions in commercially available experiment manuals, e.g. Gene Manual, Kodansha Co., Ltd.; Methods for Experiments in Gene Manipulation, edited by Yasutaka Takagi, Kodansha Co., Ltd.; Molecular Cloning, Cold Spring Harbor Laboratory (1982); Molecular Cloning, 2nd ed., Cold Spring Harbor Laboratory (1989); Methods in Enzymol., 194 (1991); and Gene Experiments Using Yeasts, published by Yodosha Co., Ltd., Japan (1994)."

This express teaching that isolation, sequencing and expression of the recombinant protein is routine in the art would motivate the use of these routine techniques to characterize and analyze the protein disclosed in Genbank AF045938 in order to determine how this protein impacts fluroquinolone resistance in Mycobacterium (see Genbank AF045938).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1637